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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/829,504	04/21/2004	David Epstein	23239-558A (ARC-58A)	7640

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MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C
ONE FINANCIAL CENTER
BOSTON, MA 02111

EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/829,504	EPSTEIN ET AL.	
	Examiner	Art Unit	
	Richard Schnizer	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 August 2008 and 17 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7,8,10,11,13-60 and 64* is/are pending in the application.

4a) Of the above claim(s) *1,2,17-46 and 52-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,7,8,10,13,47-51 and 64* is/are rejected.

7)☐ Claim(s) *11 and 14-16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 8/1/08.

Clams 4-6, 9, 12, and 61-63 were canceled and claim 64 was added.

Claims 1-3, 7, 8, 10, 11, 13-60, and 64 are pending.

Claims 1, 2, 17-46, and 52-60 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 1/24/07.

Applicant has listed claims 8 and 10 as "Withdrawn". The Examiner has not withdrawn these claims from consideration, and they read on the elected invention. Accordingly, they are properly listed as "Previously Presented".

Claims 3, 7-11, 13-16, 47-51, and 64, and SEQ ID NOS: 12-16, are under consideration in this Office Action.

Applicant's amendments and arguments overcame the objections to the claims and specification, and placed the application in compliance with 37 CFR 1.821 through 1.825.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is rejected because it depends from cancelled claim 9.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 7, 8, 13, 48, and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gorenstein et al (US 20040265912).

Gorenstein taught a pharmaceutical composition comprising concatenated thioaptamers directed against nuclear regulatory factors, wherein the aptamers also comprise a pathogen-associated molecular pattern antigen such as a CpG molecule.

More specifically, at paragraph 27 Gorenstein taught that the thioaptamers of the may be an adjuvant that forms part of a vaccine, and when used as a vaccine, that thioaptamer adjuvant may also include at least one antigen. The antigen may be a CpG molecule.

Accordingly, Gorenstein taught thioaptamer adjuvants that can be directed against a nuclear regulatory factor, and that can also contain a CpG molecule. Such

thioaptamer would be expected to be able to bind to the nuclear regulatory factor as well as to tlr9 receptors which bind CpG motifs.

Gorenstein did not exemplify any specific immunostimulatory CpG molecule, or a specific aptamer comprising a first sequence capable of binding a first target and a second sequence comprising an immunostimulatory CpG motif of the sequence rCGyy that is capable of binding a second target. However, Gorenstein did teach that CpG motifs have a general structure of two 5' purines, an unmethylated CPG, and two 3' pyrimidines (see paragraph 126).

It would have been obvious to one of ordinary skill in the art at the time of the invention to construct an thioaptamer adjuvant comprising a moiety directed against a nuclear regulatory factor and a moiety comprising a CpG motif because Gorenstein suggested that this should be done. While Gorenstein did not suggest a specific CpG motif for inclusion into the thioaptamer, Gorenstein did disclose that CpG motifs have a general structure of two 5' purines, an unmethylated CPG, and two 3' pyrimidines. Accordingly it would have been obvious to one of ordinary skill in the art at the time of the invention use such a motif in the thioaptamer. Claim 64 is included in this rejection because, although Gorenstein did not explicitly teach a CpG motif of rCGTT, Gorenstein did disclose the genus rCGyy. All of the species of this genus can be instantly visualized and are considered to be exchangeable equivalents in view of the disclosure of Gorenstein. It would have been obvious to one of ordinary skill in the art at the time of the invention to use any of them as CpG molecules in the thioaptamer of Gorenstein.

Claim 47 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gorenstein et al (US 20040265912) as applied to claims 3, 7, 8, 13, 48, and 64, and further in view of any one of Raz et al (US 6,514,948), Carson et al (USD 6,610,661), or Schwartz (US 6,562,798).

Gorenstein taught a pharmaceutical composition comprising concatenated thioaptamers directed against nuclear regulatory factors, wherein the aptamers also comprise a pathogen-associated molecular pattern antigen such as a CpG molecule. See paragraphs 26, 27, 32, and 60.

Gorenstein did not exemplify any specific immunostimulatory CpG molecule.

Raz disclosed SEQ ID NO:12 as an immunostimulatory sequence. See e.g. column 10, lines 12-16.

Carson disclosed SEQ ID NO:12 as an immunostimulatory sequence. See e.g. claims 7, 44, and 55.

Schwartz disclosed SEQ ID NO: 12 as an immunostimulatory sequence. See e.g. Table 1 at column 25.

It would have been obvious to one of ordinary skill in the art at the time of the invention to select any known CpG immunostimulatory sequence to use in the inventions of Gorenstein. Absent evidence of some unexpected result, selection of a sequence is simply a matter of choosing between obvious, equivalent alternatives. It is clear from the art cited above, that SEQ ID NO: 12 was well known in the prior art as a CpG-containing immunostimulatory molecule, and so it would have been obvious to use it, or any other well known CpG molecule in the invention of Gorenstein.

Claims 49-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gorenstein et al (US 20040265912) as applied to claims 3, 7, 13, 48, and 64, and further in view of Janjic et al (US 6,229,002).

Gorenstein taught a pharmaceutical composition comprising concatenated thioaptamers directed against nuclear regulatory factors, wherein the aptamers also comprise a pathogen-associated molecular pattern antigen such as a CpG molecule. See paragraphs 26, 27, 32, and 60. The aptamers may be coupled to biodegradable, bioacceptable polymers such as polyvinylpyrrolidone (see paragraph 64).

Gorenstein did not teach coupling of aptamers to polyethylene glycol.

Janjic taught that the pharmacokinetic properties of aptamers could be improved by conjugation of high molecular weight compounds such as polyethylene glycol of molecular weight from 20-45 kDa (see column 15, lines 19-42, and column 26, lines 50-61). Janjic exemplifies 40kDa PEG at e.g. Fig. 9.

It would have been obvious to one of ordinary skill in the art at the time of the invention to attach PEG of any molecular weight in the range of 20-45 kDa to the aptamers of Gorenstein in order to obtain improved pharmacokinetic properties as taught by Janjic. In particular, Janjic exemplified 40 kDa PEG.

Response to Arguments

Applicant's arguments filed 4/17/08 have been fully considered but they are not persuasive.

Applicant's arguments are based on the position that Gorenstein does not teach a single bifunctional oligonucleotide comprising an aptamer that binds a target while also comprising a CpG motif as instantly claimed. This is unpersuasive. At paragraph 27, Gorenstein states:

> "The thioaptamers of the present invention may be an adjuvant that forms part of a vaccine, such as a composition that includes one or more partially thio-modified or even concatenated aptamers that modulate an immune response. When used as a vaccine, that thioaptamer adjuvant may also include at least one antigen. In addition to the examples hereinabove, the antigen may be a pathogen-associated molecular pattern antigen, e.g., a CpG molecule".

Thus Gorenstein taught a thioaptamer that is itself an adjuvant. The thioaptamer adjuvant can form part of a vaccine, and when used as a vaccine "that thioaptamer adjuvant may also include one antigen." The antigen can be a CpG molecule. The simplest interpretation of this passage is that the thioaptamer can include a CpG molecule, i.e. as part of the thioaptamer. The simplest way to achieve this arrangement is to synthesize the aptamer such that it contained the CpG sequence. Thus Gorenstein fairly disclosed an aptamer directed to a target, wherein that aptamer also contains a CpG motif. Even if one does not interpret Gorenstein to disclose an aptamer comprising a CpG motif, it still would have been obvious to one of ordinary skill at the time of the invention to make an aptamer containing a CpG motif, because it would be a simple, efficient way to produce an adjuvant comprising both an aptamer and a CpG motif.

For these reasons the rejections are maintained.

Conclusion

No claim is allowed. Claims 11 and 14-16 are objected to because they depend from a rejected claim(s), but would be allowable if rewritten in independent form with all ofhte limitations of the claim(s) from which they depend.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, James (Doug) Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Richard Schnizer/
Primary Examiner, Art Unit 1635